

PATENT ABSTRACTS OF JAPAN

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(54) SOLUTION FOR INTERNAL ORGANS TO BE TRANSPLANTED

(57)Abstract:

PURPOSE: To provide a solution for the internal organs to be transplanted which enables perfusion and storage for a long period of time without any damage in the functions of the organs.

CONSTITUTION: The solution for internal organs to be transplanted contains, in 1,000ml aqueous solution, 50 to 240mM of trehalose, 10 to 40mM of Na⁺, 4 to 140mM of K⁺, 0 to 4mM of Mg⁺⁺, 0 to 2mM of Ca⁺⁺, 12 to 65mM of H₂PO₄⁻ or HPO₄⁻⁻, 15-150mM of Cl⁻, HCO⁻, CO₃⁻⁻, organic acid or organic acid anion, and 0 to 80g of hydroxyethylstarch, and has 270 to 450mOsm/l osmotic pressure and pH 7 to 8.

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CLAIMS

[Claim(s)]

[Claim 1] The solution for transplants with which the following component is contained within the limits of the following at least among 1000ml water solution, and osmotic pressure is characterized by pH being 7-8 by 270 - 450 mOsm/l.

Trehalose 50-240mM Na⁺ 10-140mM K⁺ 4-140mM Mg⁺⁺ 0- 4mM calcium⁺⁺ 0- 2mM H₂ PO₄ - Or HPO₄⁻⁻ 12-65mM Cl⁻, HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 15 - 150mM hydroxyethyl starch 0-80g

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Industrial Application] This invention relates to the solution which uses the organ for transplantation perfusion or since it saves in more detail about the solution for transplants.

[0002]

[Description of the Prior Art] Euro which contains potassium chloride, a potassium dihydrogenphosphate, the potassium phosphate, a sodium hydrogencarbonate, and grape sugar in one of the solutions for transplants most often conventionally used in the West - Collins (Euro-Collins) There is liquid. However, although this solution can be used for the high kidney of the functional maintenance force, about other organs, it cannot be said to be enough [the protective action to the denaturation of a cell], but has the problem that the maintenance time amount of an organ function is short. Hydroxyethyl starch was contained as sodium lactobionate, a raffinose, and a colloid osmotic agent as a non-penetrating agent, and the electrolytic solution and UW liquid (JP,1-246201,A) with which the adenosine, the insulin, etc. were further added in consideration of the energy metabolism of a cell were recently developed. However, this solution has a difficulty in galenical pharmacy-stability and has problems, such as needing cold storage.

[0003]

[Problem(s) to be Solved by the Invention] Therefore, in the organ for transplantation, the technical problem of this invention is perfusion or a solution for saving, is excellent in a maintenance operation of an organ function, and is to offer a solution stable in galenical pharmacy moreover.

[0004]

[Means for Solving the Problem] this invention persons were able to complete this invention which solves the above-mentioned technical problem, as a result of taking lessons from those combination and blending ratio of coal and inquiring wholeheartedly using various electrolytes, osmoregulating chemicals, colloid osmotic agents, and cell membrane stabilizers.

[0005] That is, this invention contains the following component within the limits of the following at least among 1000ml water solution, and osmotic pressure offers the solution for transplants characterized by pH being 7-8 by 270 - 450 mOsm/l.

Trehalose 50-240mM Na⁺ 10-140mM K⁺ 4-140mM Mg⁺⁺ 0- 4mM calcium⁺⁺ 0- mM H₂ PO₄ - Or HPO₄⁻⁻ 12-65mM Cl⁻, HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 15 - 150mM hydroxyethyl starch 0-80g [0006] It will be as follows if the presentation range of the more desirable embodiment of this invention (inside of 1000ml water solution) is shown. Trehalose 100-210mM Na⁺ 20-120mM K⁺ 20-130mM Mg⁺⁺ 0- 2mM calcium⁺⁺ 0- mM H₂ PO₄ - Or HPO₄⁻⁻ 20- 60mM Cl⁻, HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 20 - 120mM hydroxyethyl starch 20- The more desirable range of osmotic pressure of 40g is 270 - 380 mOsm/l again.

[0007] Although three sorts of alpha and alpha-trehalose, alpha, and beta-trehalose and beta, and beta-trehalose exist in the trehalose in the above-mentioned component, it is alpha and alpha-trehalose which exists naturally more preferably. Moreover, the above-mentioned hydroxyethyl starch is the thing of the range of 0.4-0.8, the thing of 200000-900000 is [average molecular weight] desirable still more desirable, and, as for it, whenever [permutation] is the thing of 350000-800000.

[0008] As the above-mentioned organic acid, a gluconic acid, a lactic acid, an acetic acid, a propionic acid, beta-hydroxybutyric acid, a citric acid, etc. can be illustrated, and the above sodium salt of an organic acid or potassium salt, a sodium chloride, potassium chloride, a magnesium chloride, a calcium chloride, a sodium dihydrogenphosphate, a potassium dihydrogenphosphate, disodium hydrogenphosphate, the potassium phosphate, a sodium hydrogencarbonate, a potassium hydrogencarbonate, a sodium carbonate, potassium carbonate, etc. can be illustrated as a concrete electrolyte for prescribing the above-mentioned anion and a cation.

[0009] The solution for organ transplantations of this invention can contain cell activators, such as other additives, for example, an active oxygen elimination agent, and ATP, an antibiotic, etc.

[0010] The solution for transplants of this invention can be easily manufactured based on the well-known transfusions manufacture approach.

[0011]

[Function] The solution for transplants of this invention is excellent in the protective action and edema depressant action of an organ cell, and can maintain the organ function for a long time. Moreover, an unstable compound like the insulin of UW liquid component is not used for the solution for transplants of this invention, but it is stable in galenical pharmacy.

[0012]

[Example]

After dissolving alpha and alpha-trehalose 35g, 1.12g of potassium chloride, 2.05g of potassium dihydrogenphosphates, and 7.4g of potassium phosphate in 800ml of distilled water of 50 degrees C of example 1 abbreviation, 0.84g of sodium hydrogencarbonates and distilled water were added, and the whole quantity was set to 1000ml. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 271 mOsm/l and pH7.46 was obtained.

[0013] After dissolving alpha and alpha-trehalose 70g, 1.12g of potassium chloride, 2.05g of potassium dihydrogenphosphates, and 7.4g of potassium phosphate in 800ml of distilled water of 50 degrees C of example 2 abbreviation, 0.84g of sodium hydrogencarbonates and distilled water were added, and the whole quantity was set to 1000ml. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 373 mOsm/l and pH7.42 was obtained.

[0014] Distilled water was added and the whole quantity was set to 1000ml, after dissolving alpha and alpha-trehalose 41g, 30g (whenever [average-molecular-weight 429000 and permutation] 0.55) of hydroxyethyl starch, 21.81g of sodium gluconate, 0.885g of potassium dihydrogenphosphates, and

3.222g of potassium phosphate in 800ml of distilled water of 50 degrees C of example 3 abbreviation. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 366 mOsm/l and pH7.35 was obtained. [0015] Distilled water was added and the whole quantity was set to 1000ml, after dissolving alpha and alpha-trehalose 41g, hydroxyethyl starch (whenever [average-molecular-weight 429000 and permutation] 0.55), 4.362g of sodium gluconate, 20.263g of potassium gluconate, 0.885g of potassium dihydrogenphosphates, and 3.222g of potassium phosphate in 800ml of distilled water of 50 degrees C of example 4 abbreviation. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 370 mOsm/l and pH7.37 was obtained.

[0016] The pulmo-sinister orthotopic-graft way was given using the crossbred adult dog, and the effectiveness of preservation in the perfusion list of the organ by the solution for this invention transplants was investigated.

[0017] 2 with which height and weight agree more 34 mongrels with an example of trial 1 approach weight of 7.6-13.2kg ** (an organ supply dog and this acceptance dog) It was made 1 set, considered as 17 sets, and divided into three groups (5 sets of I groups, 6 sets of II groups, and III group 6 group) at random, and the following experiments were presented.

[0018] First, after anesthetizing an organ supply dog by halothane, according to the drip method, perfusion of the 8-10-degree C test solution (it is [group / I] said Euro to example 2 liquid and an III group in example 1 liquid and II group - Collins liquid is used) was carried out under [left pulmonary artery] the condition of 50 ml/kg and 50cmH2 O. It extracted after perfusion, without separating the pulmo sinister from the heart, and immersion preservation was carried out at 500ml of these 8-10-degree C test solution. It excised under anesthesia of the pulmo sinister of an organ acceptance dog 12 hours after, and only the pulmo sinister of preservation was transplanted according to the vice method. Reperfusion of the blood was carried out, the clamp stop of the right pulmonary artery was carried out for every progress for 40 minutes, 70 minutes, and 130 minutes, and arterial oxygen tension and a pulmo-sinister arterial blood pressure were measured each time according to the conventional method.

[0019] Next, beneficial death of the organ acceptance dog was carried out, the sample was taken, respectively from the up lobe of the lung and lower lobe of the lung of transplantation lungs, and hematoxylin eosin staining was carried out to pathological findings. About the remaining up lobe of the lung and each lower lobe of the lung, the weight before desiccation (wet weight) and the weight after an oven drying (dry weight) were measured, and it asked for (wet weight)/(dry weight).

[0020] The measurement result of arterial oxygen tension was shown in the result table 1. After 130 minutes is often maintained and the transplantation pulmonary ventilatory capacity of the solution use group for this invention transplants (I group, II group) is a comparison group, i.e., Euro. - It turned out that that of a Collins liquid administration group (III group) is excelled intentionally.

[0021]

[Table 1]

[0022] Although the arterial-pressure-determination result of transplantation lungs was shown in Table 2, a significant difference is accepted in 3 between groups, and it is inside **. However, II group, I group, and III The low inclination was accepted in order of the group.

[0023]

[Table 2]

[0024] (Wet weight)/(dry weight) was computed to Table 3 as one of the indexes reflecting extent of the edema of transplantation lungs, and the result was shown in it. Like the above, although the significant difference was not accepted in 3 between groups, they are I group, II group, and III. The inclination for extent of an edema to be low was accepted in order of the group.

[0025]

[Table 3]

[0026] It was lung structure with all examples almost normal about I group and II group as a result of sample observation of hematoxylin eosin staining. However, III About the group, the critical remaining edema nature change partial to one example was accepted in five examples among six examples.

[0027] 2 with which height and weight agree more 22 mongrels with an example of trial 2 approach weight of 7.7-12.9kg ** (an organ supply dog and this acceptance dog) Make it 1 set and it considers as 11 sets. It divided into two groups (5 sets of IV groups, 6 sets of V groups) at random, and immersion preservation of the heart and the pulmo sinister was carried out like the example 1 of a trial (it is Euro to example 3 liquid and V group in IV group - Collins liquid is used). 20 hours after, the pulmo sinister was transplanted, reperfusion of the blood was carried out, and arterial oxygen tension and a pulmonary artery pressure were measured for every progress for 40 minutes, 70 minutes, and 130 minutes. In addition, after 130-minute progress, it measured also about the vascular resistance of the pulmo sinister. Furthermore, hematoxylin eosin staining of the pulmo-sinister sample was carried out like the example 1 of a trial, and it asked for remaining (wet weight)/(dry weight).

[0028] The measurement result of arterial oxygen tension was shown in Table 4. After 130 minutes is often maintained and the transplantation pulmonary ventilatory capacity of the solution use group for this invention transplants (IV group) is a comparison group, i.e., Euro. - It turned out that that of a Collins liquid administration group (V group) is excelled intentionally.

[0029]

[Table 4]

[0030] The arterial-pressure-determination result of transplantation lungs was shown in Table 5. Although the significant difference was not accepted in 2 between groups, the inclination for the arterial blood pressure of IV group to be lower than that of V group was accepted.

[0031]

[Table 5]

[0032] The vascular resistance measurement result of the transplantation pulmo sinister was shown in Table 6. It turned out that extent of the angiosclerosis denaturation of IV group is more nearly intentionally [than that of V group] low.

[0033]

[Table 6]

[0034] (Wet weight)/(dry weight) was computed to Table 7, and the result was shown in it. It turned out that extent of the edema of IV group is more nearly intentionally [than that of V group] low.

[0035]

[Table 7]

[0036] It was lung structure with all examples almost normal about IV group as a result of sample observation of hematoxylin eosin staining. However, about V group, a critical edema nature change

was accepted in all examples.

[0037] From the above test result, it became clear that the solution for this invention transplants showed the effectiveness excellent in organ functional maintenance. Especially, it is K+. Concentration is Na+. It turned out that the solution (example 3 liquid) which added hydroxyethyl starch below in abbreviation one half of concentration shows still more remarkable effectiveness by preservation for 20 hours.

[0038]

[Effect of the Invention] According to this invention, perfusion and prolonged preservation can be performed without spoiling the clue function of the organ for transplantation, and, moreover, the solution for transplants stable in galenical pharmacy can be offered.

TECHNICAL FIELD

[Industrial Application] This invention relates to the solution which uses the organ for transplantation perfusion or since it saves in more detail about the solution for transplants.

PRIOR ART

[Description of the Prior Art] Euro which contains potassium chloride, a potassium dihydrogenphosphate, the potassium phosphate, a sodium hydrogencarbonate, and grape sugar in one of the solutions for transplants most often conventionally used in the West - Collins (Euro-Collins) There is liquid. However, although this solution can be used for the high kidney of the functional maintenance force, about other organs, it cannot be said to be enough [the protective action to the denaturation of a cell], but has the problem that the maintenance time amount of an organ function is short. Hydroxyethyl starch was contained as sodium lactobionate, a raffinose, and a colloid osmotic agent as a non-penetrating agent, and the electrolytic solution and UW liquid (JP,1-246201,A) with which the adenosine, the insulin, etc. were further added in consideration of the energy metabolism of a cell were recently developed. However, this solution has a difficulty in galenical pharmacy-stability and has problems, such as needing cold storage.

EFFECT OF THE INVENTION

[Effect of the Invention] According to this invention, perfusion and prolonged preservation can be performed without spoiling the clue function of the organ for transplantation, and, moreover, the solution for transplants stable in galenical pharmacy can be offered.

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] Therefore, in the organ for transplantation, the technical problem of this invention is perfusion or a solution for saving, is excellent in a maintenance operation of an organ function, and is to offer a solution stable in galenic pharmacy moreover.

MEANS

[Means for Solving the Problem] this invention persons were able to complete this invention which solves the above-mentioned technical problem, as a result of taking lessons from those combination and blending ratio of coal and inquiring wholeheartedly using various electrolytes, osmoregulating chemicals, colloid osmotic agents, and cell membrane stabilizers.

[0005] That is, this invention contains the following component within the limits of the following at least among 1000ml water solution, and osmotic pressure offers the solution for transplants characterized by pH being 7-8 by 270 - 450 mOsm/l.

Trehalose 50-240mM Na⁺ 10-140mM K⁺ 4-140mM Mg⁺⁺ 0- 4mM calcium⁺⁺ 0- mM H₂ PO₄ - Or HPO₄⁻⁻ 12-65mM Cl⁻, HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 15 - 150mM hydroxyethyl starch 0-80g [0006] It will be as follows if the presentation range of the more desirable embodiment of this invention (inside of 1000ml water solution) is shown.

Trehalose 100-210mM Na⁺ 20-120mM K⁺ 20-130mM Mg⁺⁺ 0- 2mM calcium⁺⁺ 0- mM H₂ PO₄ - Or HPO₄⁻⁻ 20- 60mM Cl⁻, HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 20 - 120mM hydroxyethyl starch 20- The more desirable range of osmotic pressure of 40g is 270 - 380 mOsm/l again.

[0007] Although three sorts of alpha and alpha-trehalose, alpha, and beta-trehalose and beta, and beta-trehalose exist in the trehalose in the above-mentioned component, it is alpha and alpha-trehalose which exists naturally more preferably. Moreover, the above-mentioned hydroxyethyl starch is the thing of the range of 0.4-0.8, the thing of 200000-900000 is [average molecular weight] desirable still more desirable, and, as for it, whenever [permutation] is the thing of 350000-800000.

[0008] As the above-mentioned organic acid, a gluconic acid, a lactic acid, an acetic acid, a propionic acid, beta-hydroxybutyric acid, a citric acid, etc. can be illustrated, and the above sodium salt of an organic acid or potassium salt, a sodium chloride, potassium chloride, a magnesium chloride, a calcium chloride, a sodium dihydrogenphosphate, a potassium dihydrogenphosphate, disodium hydrogenphosphate, the potassium phosphate, a sodium hydrogencarbonate, a potassium hydrogencarbonate, a sodium carbonate, potassium carbonate, etc. can be illustrated as a concrete electrolyte for prescribing the above-mentioned anion and a cation.

[0009] The solution for organ transplantations of this invention can contain cell activators, such as other additives, for example, an active oxygen elimination agent, and ATP, an antibiotic, etc.

[0010] The solution for transplants of this invention can be easily manufactured based on the well-known transfusions manufacture approach.

OPERATION

[Function] The solution for transplants of this invention is excellent in the protective action and edema depressant action of an organ cell, and can maintain the organ function for a long time. Moreover, an

unstable compound like the insulin of UW liquid component is not used for the solution for transplants of this invention, but it is stable in galenical pharmacy.

EXAMPLE

[Example]

After dissolving alpha and alpha-trehalose 35g, 1.12g of potassium chloride, 2.05g of potassium dihydrogenphosphates, and 7.4g of potassium phosphate in 800ml of distilled water of 50 degrees C of example 1 abbreviation, 0.84g of sodium hydrogencarbonates and distilled water were added, and the whole quantity was set to 1000ml. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 271 mOsm/l and pH7.46 was obtained.

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[0018] First, after anesthetizing an organ supply dog by halothane, according to the drip method, perfusion of the 8-10-degree C test solution (it is [group / I] said Euro to example 2 liquid and an III group in example 1 liquid and II group - Collins liquid is used) was carried out under [left pulmonary artery] the condition of 50 ml/kg and 50cmH2 O. It extracted after perfusion, without separating the pulmo sinister from the heart, and immersion preservation was carried out at 500ml of these 8-10-degree C test solution. It excised under anesthesia of the pulmo sinister of an organ acceptance dog 12

hours after, and only the pulmo sinister of preservation was transplanted according to the vice method. Reperfusion of the blood was carried out, the clamp stop of the right pulmonary artery was carried out for every progress for 40 minutes, 70 minutes, and 130 minutes, and arterial oxygen tension and a pulmo-sinister arterial blood pressure were measured each time according to the conventional method. [0019] Next, beneficial death of the organ acceptance dog was carried out, the sample was taken, respectively from the up lobe of the lung and lower lobe of the lung of transplantation lungs, and hematoxylin eosin staining was carried out to pathological findings. About the remaining up lobe of the lung and each lower lobe of the lung, the weight before desiccation (wet weight) and the weight after an oven drying (dry weight) were measured, and it asked for (wet weight)/(dry weight). [0020] The measurement result of arterial oxygen tension was shown in the result table 1. After 130 minutes is often maintained and the transplantation pulmonary ventilatory capacity of the solution use group for this invention transplants (I group, II group) is a comparison group, i.e., Euro. - It turned out that that of a Collins liquid administration group (III group) is excelled intentionally. [0021]
[Table 1]

[0022] Although the arterial-pressure-determination result of transplantation lungs was shown in Table 2, a significant difference is accepted in 3 between groups, and it is inside **. However, II group, I group, and III The low inclination was accepted in order of the group. [0023]
[Table 2]

[0024] (Wet weight)/(dry weight) was computed to Table 3 as one of the indexes reflecting extent of the edema of transplantation lungs, and the result was shown in it. Like the above, although the significant difference was not accepted in 3 between groups, they are I group, II group, and III. The inclination for extent of an edema to be low was accepted in order of the group. [0025]
[Table 3]

[0026] It was lung structure with all examples almost normal about I group and II group as a result of sample observation of hematoxylin eosin staining. However, III About the group, the critical remaining edema nature change partial to one example was accepted in five examples among six examples. [0027] 2 with which height and weight agree more 22 mongrels with an example of trial 2 approach weight of 7.7-12.9kg ** (an organ supply dog and this acceptance dog) Make it 1 set and it considers as 11 sets. It divided into two groups (5 sets of IV groups, 6 sets of V groups) at random, and immersion preservation of the heart and the pulmo sinister was carried out like the example 1 of a trial (it is Euro to example 3 liquid and V group in IV group - Collins liquid is used). 20 hours after, the pulmo sinister was transplanted, reperfusion of the blood was carried out, and arterial oxygen tension and a pulmonary artery pressure were measured for every progress for 40 minutes, 70 minutes, and 130 minutes. In addition, after 130-minute progress, it measured also about the vascular resistance of the pulmo sinister. Furthermore, hematoxylin eosin staining of the pulmo-sinister sample was carried out like the example 1 of a trial, and it asked for remaining (wet weight)/(dry weight). [0028] The measurement result of arterial oxygen tension was shown in Table 4. After 130 minutes is often maintained and the transplantation pulmonary ventilatory capacity of the solution use group for this invention transplants (IV group) is a comparison group, i.e., Euro. - It turned out that that of a Collins liquid administration group (V group) is excelled intentionally.

[0029]
[Table 4]

[0030] The arterial-pressure-determination result of transplantation lungs was shown in Table 5. Although the significant difference was not accepted in 2 between groups, the inclination for the arterial blood pressure of IV group to be lower than that of V group was accepted.
[0031]
[Table 5]

[0032] The vascular resistance measurement result of the transplantation pulmo sinister was shown in Table 6. It turned out that extent of the angiosclerosis denaturation of IV group is more nearly intentionally [than that of V group] low.
[0033]
[Table 6]

[0034] (Wet weight)/(dry weight) was computed to Table 7, and the result was shown in it. It turned out that extent of the edema of IV group is more nearly intentionally [than that of V group] low.
[0035]
[Table 7]

[0036] It was lung structure with all examples almost normal about IV group as a result of sample observation of hematoxylin eosin staining. However, about V group, a critical edema nature change was accepted in all examples.
[0037] From the above test result, it became clear that the solution for this invention transplants showed the effectiveness excellent in organ functional maintenance. Especially, it is K+. Concentration is Na+. It turned out that the solution (example 3 liquid) which added hydroxyethyl starch below in abbreviation one half of concentration shows still more remarkable effectiveness by preservation for 20 hours.

CORRECTION OR AMENDMENT

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[Procedure revision]

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[Procedure amendment 1]

[Document to be Amended] Specification

[Item(s) to be Amended] Claim

[Method of Amendment] Modification

[Proposed Amendment]

[Claim(s)]

[Claim 1] The solution for transplants with which the following component is contained within the limits of the following at least among 1000ml water solution, and osmotic pressure is characterized by pH being 7-8 by 270 - 450 mOsm/l.

Trehalose 50-240mM

Na⁺ 10-140mM

K⁺ 4-140mM

H₂PO₄⁻ or HPO₄⁻⁻ 12-65mM

Cl⁻, and HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 15-150mM

[Claim 2] Furthermore, the solution for transplants according to claim 1 which contains 80g or less of hydroxyethyl starch in said 1000ml water solution.

[Claim 3] The solution for transplants according to claim 2 whose content of said hydroxyethyl starch is 20g or more 40g or less.

[Claim 4] Furthermore, the solution for transplants according to claim 1 to 3 which contains respectively 4 or less mM and/or 2 or less mM calcium⁺⁺ for Mg⁺⁺ in said 1000ml water solution.

[Claim 5] The solution for transplants according to claim 1 to 4 which has osmotic pressure within the limits of 270 - 380 mOsm/l.

[Procedure amendment 2]

[Document to be Amended] Specification

[Item(s) to be Amended] 0002

[Method of Amendment] Modification

[Proposed Amendment]

[0002]

[Description of the Prior Art] An organ transplantation has another organization, the organization which does not require angiostomy for the purpose of removing an organ and aiming at functional recovery or transplantation (a cornea, the skin graft, a bone marrow transplantation, etc.) of a cell, and the transplantation which needs revascularization instead of a function being the organization and organ which were fallen and abolished (the Nanzando medicine great dictionary, 1990). The Euro-Collins (Euro-Collins) liquid containing potassium chloride, a potassium dihydrogenphosphate, the potassium phosphate, a sodium hydrogencarbonate, and grape sugar is in one of the solutions for transplants most often conventionally used in the West. However, although this solution can be used for the high kidney of the functional maintenance force, about other organs, it cannot be said to be enough [the protective action to the denaturation of a cell], but has the problem that the maintenance time amount of an organ function is short. Hydroxyethyl starch was contained as sodium lactobionate, a raffinose, and a colloid osmotic agent as a non-penetrating agent, and the electrolytic solution and UW liquid (JP,1-246201,A) with which the adenosine, the insulin, etc. were further added in consideration of the energy metabolism of a cell were recently developed. However, this solution has a difficulty in galenical pharmacy-stability and has problems, such as needing cold storage.

[Procedure amendment 3]

[Document to be Amended] Specification

[Item(s) to be Amended] 0005

[Method of Amendment] Modification

[Proposed Amendment]

[0005] That is, this invention contains the following component within the limits of the following at least among 1000ml water solution, and osmotic pressure offers the solution for transplants characterized by pH being 7-8 by 270 - 450 mOsm/l.

Trehalose 50-240mM

Na⁺ 10-140mM

K⁺ 4-140mM

H₂PO₄⁻ or HPO₄⁻⁻ 12-65mM

Cl⁻, and HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 15-150mM

However, it is desirable when 80g or less of hydroxyethyl starch (henceforth "HES") is made to contain in 1000ml water solution if needed. Moreover, less than [Mg⁺⁺4mM] and/or less than [calcium⁺⁺2mM] other than the above-mentioned sodium ion or calcium ion may be made to contain also as an electrolytic cation.

[Procedure amendment 4]

[Document to be Amended] Specification

[Item(s) to be Amended] 0006

[Method of Amendment] Modification

[Proposed Amendment]

[0006] It will be as follows if the presentation range of the more desirable embodiment of this invention (inside of 1000ml water solution) is shown.

Trehalose 100-210mM

Na⁺ 20-120mM

K⁺ 20-130mM

H₂PO₄⁻ or HPO₄⁻⁻ 20-60mM

Cl⁻, and HCO₃⁻, CO₃⁻⁻, an organic acid, or organic-acid anion 20-120mM

Furthermore, when making the solution for transplants of this invention contain any one or more sorts in Mg^{++} , calcium $^{++}$, and hydroxyethyl starch, desirable contents (inside of 1000ml water solution) are less than [$Mg^{++}2mM$], less than [calcium $^{++}1mM$], and hydroxyethyl starch 20-40g, respectively. Moreover, the more desirable range of osmotic pressure is 270 - 380 mOsm/l.

[Procedure amendment 5]

[Document to be Amended] Specification

[Item(s) to be Amended] 0015

[Method of Amendment] Modification

[Proposed Amendment]

[0015] Example 4

Distilled water was added and the whole quantity was set to 1000ml, after dissolving alpha and alpha-trehalose 41g, 30g (whenever [average-molecular-weight 429000 and permutation] 0.55) of hydroxyethyl starch, 4.362g of sodium gluconate, 20.263g of potassium gluconate, 0.885g of potassium dihydrogenphosphates, and 3.222g of potassium phosphate in 800ml of about 50-degree C distilled water. This was filtered immediately, to the carboy, after restoration and sealing, wet sterilization was carried out and the solution for transplants of osmotic-pressure 370 mOsm/l and pH7.37 was obtained.

[Procedure amendment 6]

[Document to be Amended] Specification

[Item(s) to be Amended] 0016

[Method of Amendment] Modification

[Proposed Amendment]

[0016] The pulmo-sinister orthotopic-graft way was given using the crossbred adult dog, and the effectiveness of preservation in the perfusion list of the organ by the solution for this invention transplants was investigated. In addition, the constituent concentration of the solution for transplants of examples 1-4 is as having indicated to the below-mentioned table 8.

[Procedure amendment 7]

[Document to be Amended] Specification

[Item(s) to be Amended] 0036

[Method of Amendment] Modification

[Proposed Amendment]

[0036] It was lung structure with all examples almost normal about IV group as a result of sample observation of hematoxylin eosin staining. However, about V group, a critical edema nature change was accepted in all examples. The constituent concentration of the solution of the above example is as in Table 8.

[Table 8]
